Multi source analysis of DC MEG data during visually evoked migraine

S.M. Bowyer[1], S.K. Aurora[1], D.E. Burdette[1], J.E. Moran[1], N. Tepley[1,2], and K.M.A. Welch[3]

[1]*Henry Ford Hospital, Detroit, Michigan USA;* [2]*Oakland University, Rochester, Michigan USA*
[3]*University of Kansas School of Medicine, Kansas City, Kansas USA*

1 Introduction

The magnetoencephalographic (MEG) signals arising during migraine are not represented by a single current dipole but by a continuous band of depolarizing neurons that propagates like a wave-front across the cortex. This wave is hypothesized to be an underlying event in migraine, spreading cortical depression (SCD) [1]. Wijesinghe et al [2] used a summation of individual current dipoles to model MEG signals expected to arise from propagation of SCD through a human sulcus. Bowyer [3] used a computer simulation of a band of single current dipoles across the surface of a cortical strip to cross correlate to the actual MEG signals arising from SCD in animal model. The complexity of modeling MEG signals arising from an extended or continuum source requires use of more complex source analysis. In this work, Two Dimensional Inverse Imaging (2DII) [4], a computer modeling technique involving multiple source analysis, was applied to MEG data from a visually evoked migraine-with-aura subject and a control subject. 2DII was also applied to a M+A subject experiencing an aura.

2 Methods

2.1 Patient studies

Neuromagnetic fields were measured in three subjects; one migraine patient, one ictal migraine patient (experiencing spontaneous migraine-with-aura) and one control individual (no history of migraine headaches). The control and the migraine patient not experiencing a headache or aura were studied during visual stimulation of the occipital cortex. A 148-channel Neuromagnetometer (4D Neuro-imaging WH2500) was used to collect the data.

The ictal migraine patient was monitored for 15 minutes while his visual aura persisted. The migraine patient and the control were monitored for 18 minutes during presentation of visual stimulus.

The stimulus pattern was projected into the shielded room, and viewed on an opaque white projection screen. The stimulus consisted of a checkerboard pattern which had a 50 degree radius and 5 degree check size that alternated black and white at 8 Hz. All data were collected on a Sun Ultra 60 workstation, digitized at 290.64 samples per second, band passed at 0-50 Hz.

MRI scans were performed on all of the subjects in the Henry Ford Hospital MRI facility. The MRI scan was used to co-register the MEG data to specific locations in the cortex of each individual. (The techniques for co-registration of MEG and MRI are well established and used in all of our clinical MEG studies.) This allowed for precise localization of the anatomical area of cortical activation. MRI scan parameters were: coronal T1 images, 124 slices, and 256x256 matrix, covering the entire skin surface of the head.

2.2 Data Analysis

The Neuromagnetic data collected during the passive viewing of circular checker board pattern stimulus were analyzed for DC MEG shifts that occur when neurons are depolarizing in a propagating manner. The alternating checkerboard stimulus has been used to successfully stimulate migraine auras in previous migraine studies [6]. Data were filtered 0.001-50 Hz to remove any equipment drift which was coherent in all 148 channels. The data were then exported to Matlab, and decimated from 254 to 11 samples per second to simplify computer manipulations. These two steps did not affect the slowly varying DC shifts, which occur over minutes. Data were normalized to compensate for difference in head sizes of the subjects and the different distances of the head to the sensors. A local sphere was fit to the back of the digitized head shape, and the distance from the surface of the sphere to pickup coils was calculated for each posterior channel. We assumed that the source of the field was located on the surface of the brain, directly under the detector; this allowed the use a $1/r^2$ fall-off factor to adjust the amplitudes so that all data sets were normalized to a 4 cm distance from scalp to pickup coil.

Equivalent current dipole (ECD) source analysis was attempted but the correlations and goodness of fits were very poor.

Two Dimensional Inverse Imaging (2DII), developed in this lab, for imaging the cortical distribution of neuronal activity was applied to the data [4]. This technique was utilized because the underlying sources were expected to be from extended source structures within the occipital cortex rather than a single compact source for which the single ECD is adequate. The MRI was used as a constraint for the source space solutions. The 2DII results were then displayed on the subjects MRI.

3 Results

3.1 DC shifts

Slow MEG signal shifts were observed in M+A subjects [5]. Our results show that there are differences between the DC MEG fields of controls (amplitude of shifts <9pT) and M+A subjects (average amplitude of shifts 37 $\pm$ 17 pT).

3.2 2DII

Cortical activation maps showed large areas of multiple activated patterns in the occipital region of the spontaneous migraine subject, which is consistent with SCD propagating into and out of the folded sulci of a real brain. (Fig. 1). The aura was in progress when the MEG recordings were started. Large amplitude DC MEG signals were seen arising from the right hemisphere. The concurrent negative and positive deflections indicate that there is neuroelectric activity occurring under these channels. 2DII was applied to the time segment 50-250 seconds. The average 2DII results of this time segment are shown in Figure1.

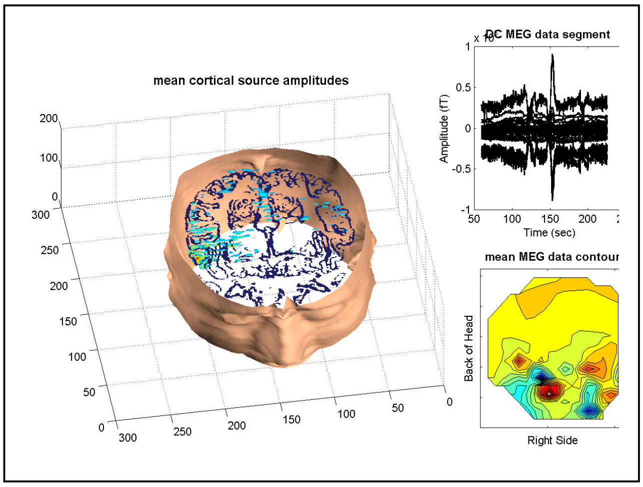

Figure 1: *2DII localization of the location of DC MEG shifts during a spontaneous visual aura on to MRI, Data segment plot, and Mean data contour for 200 seconds are shown.*

Figure 2 displays the 2DII localization of DC MEG shifts during a visually evoked migraine aura. DC MEG shifts were detected 150 seconds after stimulus onset and continued for entire time period of MEG recording. The pattern of shifting DC MEG signals seen in

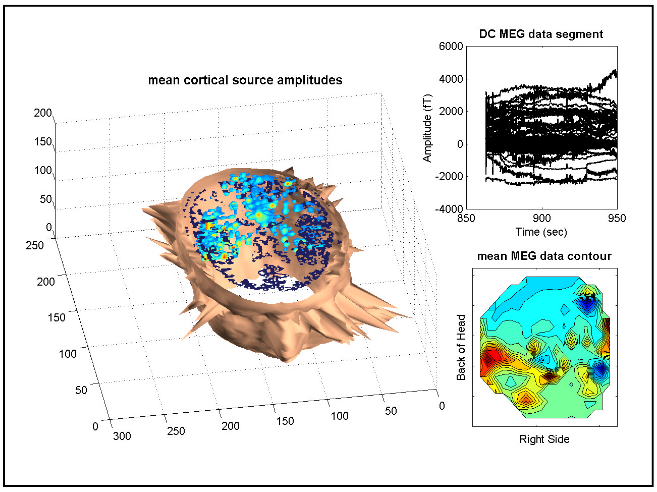

Figure 2: *2DII localization of the location of DC MEG shifts during a visual evoked migraine aura. External distortion of the patient skull is due to artifacts in the MRI data used to generate the 3D surface*

association with spontaneous migraine are similar to those seen with induced migraine. 2DII was applied to the time segment 850-950 seconds, where shifts were very similar to DC MEG shifts seen in the spontaneous M+A subject. The average contour plot for 100 seconds is displayed along with the localization of cortical activity on the MRI scan, and the time segment of MEG data (Fig. 2). Multiple areas of cortical activation are seen in the occipital area and extending out toward the right temporal area.

2DII was also applied to the 200 seconds of MEG data from a control subjects during visual stimulation, but all that was observed was the visual evoked activity, which is normally found during visual stimulation. Very little variation in the average cortical activation maps over the entire 1800 seconds were found in the control subjects. The average contour for the time segment displayed is shown (Fig.3)

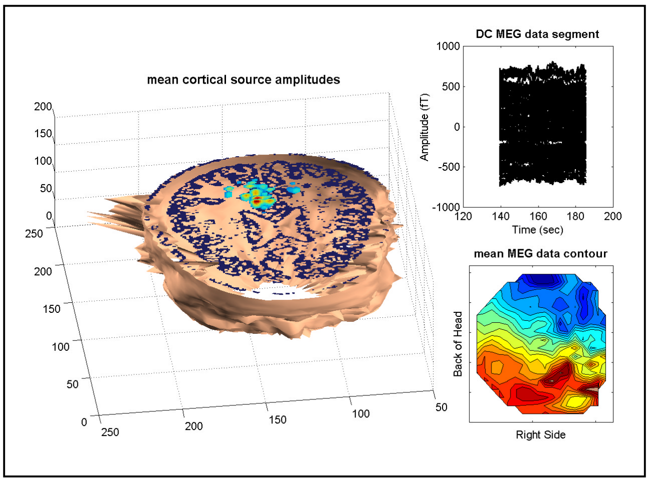

Figure 3: *2DII analysis of MEG signals during visual stimulation of a control subject on to MRI, 80 second data segment, and Mean data contour for 200 seconds are shown.*

4 Discussion

Results of the 2DII technique showed that the activity in normal control subjects was static throughout the length of the study with activity localized to the primary visual cortex. In the visually stimulated M+A subject 2DII localized the activity to the calcarine fissure and areas in the right parietal cortex. This 2DII pattern of activity is consistent with an SCD-like event occurring in either the primary visual cortex or the second visual areas in the parietal cortex. This pattern of activity may be the band of hyperexcited neurons depolarizing that is hypothesized to occur during the aura of migraine. In the spontaneous M+A patient there was no active stimulation of the primary visual cortex, therefore activity at this site may be due to feedback from an SCD-like event in the parietal cortex or the site of an SCD-like event. This analysis helped understand the neuronal activity occurring during the migraine aura.

Our results provide further support to the hypothesis that migraine subjects have more excitable cortices than normal controls. This hyperexcitability may lead to the cascade of depolarizing neurons, known as spreading cortical depression.

There are measurable differences in MEG recordings between migraine and non-migraine subjects. Neuromagnetic signals from migraine aura subjects were multiphasic and intricate. Therefore a simple ECD did not work since the MEG signals were from an extended propagating source rather than a local static source on the cortical surface. Propagation of a wave of hyperexcitation across a convoluted cortex gives rise to complex field patterns due to the propagation in different directions across multiple sulci making the interpretation of MEG signals from SCD-like events non-trivial. The results here show that the neuronal activity during migraine-with-aura can be modeled by 2DII multiple source analysis.

Combining the analytical results from 2DII MEG with other functional imaging modalities such as EEG, fMRI, PET, and SPECT, each co-registered with the subject's MRI, will help produce a more detailed picture of the underlying biophysics occurring in the human brain during specific neurological disorders.

Acknowledgements

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